



Reply to Fiscella: The phases of biomedical research should be studied to optimize health outcomes

We thank Kevin Fiscella for his comments (1) on our report (2). Biomedical science is generally broken into early phases, consisting of basic research and applied translational research or therapeutic development, and late phases, including comparative effectiveness, implementation, and dissemination research (3). Fiscella describes the importance of late-phase research in enabling the widespread adoption of proven interventions, and asserts that increased support of late-phase research is key to improving health outcomes (1). We do not disagree, but note that in our analysis, we used both new therapeutics and life expectancy as biomedical research outcome measures (2). Although much of the value of late-phase research is not captured by the number of new drugs, this value is expected to be reflected in life expectancy gains.

Fiscella also advocates a “pull-back” from obvious translation in early-phase research to encourage creativity (1). We agree that an early focus on translation could squelch the unbridled curiosity that can lead to transformative discovery. The development of optogenetics by Karl Deisseroth and others, which was built upon the decades-earlier discovery of light-responsive microbial proteins, provides one example in support of undirected basic research (4). Basic science is the foundation for most phases of biomedical research. Without prior investments in basic science, there would be much less translational research to pursue and many fewer proven interventions to implement.

Translational research, however, is also critical to improving health outcomes (5). It is clear that each phase of biomedical research provides significant value to the biomedical research enterprise. This leads to a very important, but very difficult question: Given limited funding, how should resources be allocated between the different phases of biomedical research to best maximize sustainable long-term outcomes? To our knowledge, this is still an open question that deserves further study.

Our analysis does not distinguish between the various phases of research because these are intimately intertwined to produce positive outcomes for human health. Instead, we take an aerial view of the biomedical research enterprise to compare overall inputs and outputs with measurable outcomes. We discuss a number of potential explanations for the growing input-outcome disparity in biomedical research that have been proposed in the literature (2). As Fiscella details for late-phase research (1), every research phase faces unique challenges and barriers to success that need to be studied to maximize impact.

Any potential reforms designed to improve outcomes of a particular phase of biomedical research should be evidence-based and studied in the context of the entire biomedical research enterprise. We expect that this will require a comprehensive framework for measuring outcomes and the collaboration of experts from disparate fields, and will include the variables about which Fiscella (1) is con-

cerned. In our discussion (2) we note several factors that could be contributing to the increasing inefficiencies in the delivery of certain outcomes from biomedical research. We caution against focusing on any one explanation and urge readers to consider that these factors may be acting in concert to degrade the enterprise.

Anthony Bowen^a and Arturo Casadevall^{a,b,1}
^aDepartment of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461; and ^bDepartment of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205

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- 1 Fiscella K (2015) Distinguishing phases of biomedical research is critical to improving health outcomes. *Proc Natl Acad Sci USA* 112:E6412.
 - 2 Bowen A, Casadevall A (2015) Increasing disparities between resource inputs and outcomes, as measured by certain health deliverables, in biomedical research. *Proc Natl Acad Sci USA* 112(36):11335–11340.
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The authors declare no conflict of interest.

¹To whom correspondence should be addressed. Email: acasade1@jhu.edu.